i. contains an amino acid sequence that is derived from a superantigen selected from the group consisting of staphylococcal enterotoxin A, B, C_1, C_2, D and E,

ii. has the ability to bind to a Vβ of a T cell receptor, and

iii. has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived.

REMARKS

This is a supplemental amendment in response to an Office Communication mailed February 11, 2000. A one month response time was set, making this paper timely by being filed on or before March 11, 2000.

A supplemental amendment has been made correcting an error in the amendment filed November 15, 1999. As requested by the Examiner, the amendment of "superantigen" to "superantigens" in the last line of claim 36 has now properly been presented. For the reasons presented in the amendment and response filed November 15, 1999, applicants respectfully assert that the claims are in condition for allowance. A Notice Of Allowance is therefore respectfully requested.

As indicated in the accompanying Substitute Petition To The Commissioner Under 37 C.F.R. § 1.181 From Improper Requirement For Restriction, the restriction requirement is improper as the liking feature is patentable over the prior art

In the Office Communication of February 11, 2000, the Examiner noted that Buelow teaches that amino acids 1-138 of a protein A-SEB conjugate stimulates B cells. Applicants agree that Buelow teaches that amino acids 1-138 of a protein A-SEB conjugate stimulates B cells. In fact, this was noted in Applicant's amendment and response filed November 15, 1999 (page 11, lines 8-9) and in the Petition filed November 15, 1999 (page 6, lines 13-14). The Examiner argues that Buelow, by showing that amino acids 1-138 of a protein A-SEB conjugate have activity, makes the restriction proper because it inherently anticipates the special technical feature (the conjugate of claim 14[1/]).

Applicants respectfully disagree. The special technical feature, the conjugate of claim 14, involves a superantigen conjugate in which the superantigen has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived. Buelow does not anticipate the inventive subject matter (the special technical feature and claim 14) because it is not an enabling disclosure of the inventive subject matter. In order to anticipate, prior art must provide an enabling disclosure of the anticipated subject matter. Here, the alleged anticipated subject matter is drawn to a superantigen conjugate in which the superantigen has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived. Enablement for such a conjugate requires guidance as to, for example, which regions of the superantigen to mutate (and, for example, how to mutate them) and which particular "modified" abilities to bind MHC class II antigen to expect therefrom.

[1/]In the Office Communication of February 11, 2000 the Examiner referred to claim 1 as a restricted independent claim covering the conjugate. However, we presume the intent was to refer to claim 14, as there is no pending claim 1, and restricted claim 14 is an independent claim covering the conjugate.

Buelow does not in any manner teach, disclose or suggest mutating residues in a full length superantigen in order to affect (modify) MHC Class II antigen binding. It is entirely unclear from Buelow which regions of a full length superantigen should be mutated in order to expect a mutant protein with altered MHC Class II binding. The disclosure, teaching and suggestion of Buelow all are directed solely to the *use of truncated pCA-SEB fusion proteins to map to the amino-terminal half of the molecule (residues 1-138) a minimally immunologically active domain of SEB capable of inducing proliferation and anergy in cloned human T cells expressing VB3.1* (see first paragraph of page 2, Buelow). Buelow is not aimed at identifying the MHC Class II binding domain and certainly is not aimed at identifying which residues of full length superantigens may be mutated to specifically alter Class II MHC antigen binding. Buelow provides an indication that the region encompassing residues 1-138 of SEB constitutes a functional (i.e., "immunologically active") domain of the molecule; however, the Buelow authors recognize that it remains to be determined which parts of the molecule are involved in the interactions with Class II MHC antigens and TCR molecules, for example, directly, and/or indirectly (for example by influencing the conformation of the molecule) (see Discussion section on page 6, Buelow).

Indeed, the actual data presented in Buelow makes it clear that it does not teach or predict anything about Class II MHC antigen binding. For example, F45 and E67 are known to be important for Class II MHC binding in SEB and both the Buelow 1-130 and 1-138 SEB fragments have these identical (wild-type) sequences. However, as discussed above and plainly shown in Buelow, these two proteins have dramatically differing activities; the fragment 1-130 has neither mitogenic nor tolerogenic activity, while 1-138 fragment (identical *but for* the additional eight amino acids which are not in the recognized Class II MHC binding region) has activity. Hence, there is no way that one

skilled in the art could gain any information from Buelow about which residues in superantigens are important in Class II MHC binding.

As presented in the attached Substitute Petition, Applicants respectfully assert that all claims as originally presented and currently pending (claims 14-38, 44-47 and 52-57) are patentable as a single invention. Withdrawal of the restriction requirement and examination of all claims on the merits is therefore requested.

The Examiner is encouraged to call the undersigned attorney to discuss any matters relating to this case.

Applicants respectfully petition for any extension of time necessary to render this response timely.

Please charge any fees due or credit any overpayment to the standing account of Fulbright & Jaworski L.L.P., Deposit No. 06-2375/09804877.

Respectfully submitted,

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